44 INFLUENCE OF NEONATAL NICOTINE EXPOSURE ON DEVELOPMENT OF NICOTINIC RECEPTOR SUBTYPES AND BEHAVIOUR IN ADULT MICE

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The specific binding sites for ^{3}H-nicotine in mice brain are detectable during late prenatal period and gradually increase during postnatal period from day of birth until about 28 days of age, when they reach adult level(1). The competition curves of ^{3}H-nicotine/(-)nicotine in mice cortex of 1 day and 5 days of age are best fitted to an one-site model, and in adult mice cortex, to a two-site model (1). Subchronic treatment of rat with nicotine significantly increases the number of high affinity nicotinic binding sites with a parallel increase in the proportion of high affinity binding sites compared to low affinity binding sites in rat cortex (2). The present study intended to investigate, by means of receptor binding assay and behavioural test, the influence of neonatal nicotine exposure on development of nicotinic receptor subtypes and behaviour in adult mice.

Male NMRT mice received nicotine (66 µg base/kg) twice a day (8 am. and 5 pm.) between 10-16 postnatal day. The control group received saline in the same way. Some of the mice were killed at 17 days of age, and their cortices were used for binding assay. The others were kept until adult age of 4 months, when they after behavioural test were killed and their cortices were used for binding assay. The displacement curves for ^{3}H-nicotine/(-)nicotine in control cortex of 17 days mice were best fitted to a two-site model with affinity constants of 0.38 nM (K_H) and 14 nM (K_L), respectively. A two-site model fit was also observed in control adult cortex with a K_H 3.6 nM and a K_L 1.2 µM thus about ten and hundred times higher than those for 17 days mice, respectively. Interestingly, the ^{3}H-nicotine/(-)nicotine displacement curves of nicotine treated 17 days and adult mice were best fitted to an one-site model. The affinity constant (K_D) was 2.1 nM for 17 days mice and 3.0 nM for adult. There was no difference in Bmax between nicotine treated and control adult mice. Nicotine induced behaviour was studied by using two different doses of nicotine; 40 and 80 µg nicotine base/kg body weight. The result from locomotion, rearing times and total activity showed that mice receiving nicotine between 10-16 postnatal day displayed a hypoactive condition, whereas mice receiving saline displayed a hyperactive condition. In conclusion, neonatal treatment with nicotine caused a change in the nicotinic receptors in adult animals with a loss in low affinity binding sites; it also resulted in an opposite behavioural effect of nicotine in neonatal nicotine treated animals compared to naïve animals.

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